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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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ROPES & GRAY LLP
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EXAMINER	
GUZO, DAVID	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	08/552,839	WANG ET AL.	
	Examiner	Art Unit	
	David Guzo	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 May 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *37-42,49-51 and 62-64* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *37-42,49-51 and 62-64* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/10/98*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action

As of the mailing of this Office Action, *ex parte* prosecution in Serial Number 08/552,839 is resumed.

35 USC 102 Rejections

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 37, 41 and 49-50 are rejected under 35 U.S.C. 102(e) as being anticipated by Kovesdi et al. (US 6,482,616).

Applicants claim a DNA plasmid comprising an adenoviral gene fragment E4 open reading frame ORF6 operably linked to an inducible promoter wherein the inducible promoter is a tetracycline responsive promoter. Applicants also claim a packaging cell line derived from a 293 cell that supports the growth of a mutant adenovirus defective in replication or a recombinant adenoviral vector, wherein said adenovirus or adenoviral vector comprises a transgene and a lethal deletion or mutation in two gene reqions selected from the group consisting of El, E2A, E4-ORF6 early regions, and optionally a deletion of the E3 gene region or wherein said adenovirus or adenoviral vector comprises a transgene and a lethal deletion or mutation in each of

adenovirus E1 and E4-ORF6 early region gene regions and optionally a deletion in the E3 region.

Kovesdi et al. (issued 11/19/2002, priority to 6/10/1994, see whole document, particularly Claims 1-10, Examples 8-10, paragraph bridging columns 7-8, etc.) teaches a DNA plasmid comprising a E4 ORF6 operably linked to a promoter which can be selected from an inducible promoter such as a tetracycline responsive promoter. Kovesdi et al. also teaches 293 packaging cells that support growth of mutant adenoviruses comprising a transgene and deleted in E1, E4, E2A and optionally the E3 region. Kovesdi et al. therefore teaches the claimed invention.

It is noted that claim 41 is included in this rejection while the claim from which it depends (claim 38) is not because the tetracycline responsive promoter is apparently not a cAMP response element binding protein regulated gene (see also 35 USC 112, 2nd paragraph rejection and the objection under 37 CFR 1.75(c) of claim 41 recited below).

35 USC 103(a) Rejections

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of

the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 38-40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kovesdi et al. in view of Su et al.

Applicants claim a DNA plasmid comprising an adenoviral gene fragment E4 open reading frame ORF6 operably linked to an inducible promoter wherein the inducible promoter is from a cAMP response element binding protein regulated gene such as a mouse alpha inhibin gene.

Kovesdi et al. (cited above) teaches a DNA plasmid comprising a E4 ORF6 operably linked to a promoter which can be selected from an inducible promoter. Kovesdi et al. does not teach use of the mouse inhibin promoter to drive expression of the E4 ORF6 sequence.

Su et al. (Biochem. Biophys. Res. Comm., 1992, Vol. 186, pp. 293-300, see whole article, particularly the Summary, Fig. 3, pp. 298-299) teaches the mouse alpha inhibin promoter sequence and properties of said promoter.

The ordinary skilled artisan, seeking to choose an inducible promoter to drive expression of the E4 ORF6 region in the plasmids disclosed by Kovesdi et al., would have been motivated to choose the well known mouse alpha inhibin promoter as

disclosed by Su et al. because said promoter was a well known and characterized inducible promoter. It would have been obvious for the ordinary skilled artisan to do this because Kovesdi et al. teaches that any suitable inducible promoter can be used to drive expression of adenoviral genes such as the E4 and E2a genes and Su et al. teaches the characteristics of the well known mouse alpha inhibin inducible promoter. Applicants have used a known element (mouse alpha inhibin promoter) for its known and expected function (expression of transgenes) and hence use of the alpha inhibin promoter in the claimed context would have been obvious to the ordinary skilled artisan. Given the teachings of the prior art and the level of skill of the ordinary skilled artisan at the time of applicants' invention, it must be considered, Absent evidence to the contrary, that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Claim 62 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kovesdi et al. in view of Williams et al. (US 5,686,278).

Applicants' claim a recombinant replication-defective adenovirus, wherein the genome of said adenovirus comprises at least a lethal-deletion or mutation in two gene regions selected from the group consisting of E1, E2A and E4 early gene regions, and additionally comprises a transgene under the control of the human phosphoglycerate kinase promoter, such that the replication-defective adenovirus requires for complementation *in trans* at least the E1 and E4 early gene regions, and at most requires complementation of all three gene regions.

Kovesdi et al. (cited above, see whole document, particularly Columns 6-7 and Claims 1-10, etc.) recites a recombinant replication-defective adenovirus, wherein the genome of said adenovirus comprises deletions in gene regions selected from the group consisting of E1, E2A and E4 early gene regions, and additionally comprises a transgene under the control of a promoter of choice, such that the replication-defective adenovirus requires for complementation *in trans* the E1 and E4 early gene regions, and at most requires complementation of all three gene regions. Kovesdi et al. does not recite use of the human phosphoglycerate kinase promoter to drive expression of the transgene.

Williams et al. (issued 11/11/1997, filed 3/25/1994, see whole document, particularly Column 4) teaches use of the well known human phosphoglycerate kinase (PGK) promoter to drive expression of transgenes in viral vectors.

The ordinary skilled artisan, seeking to select a suitable promoter to drive expression of a transgene in the adenoviral vectors disclosed by Kovesdi et al. would have been motivated to choose the human PGK promoter because Williams et al. teaches that the human PGK promoter could be used to drive expression of transgenes in viral vectors. It would have been obvious for the ordinary skilled artisan to do this because Kovesdi et al. teaches that any suitable promoter could be used to express the transgene in the adenoviral vectors and Williams et al. teaches that the well known human PGK promoter was usable to express transgenes in viral vectors. Applicants have used a known element (human PGK promoter) for its known and expected function (expression of transgenes) and hence use of the human PGK promoter in the

claimed context would have been obvious to the ordinary skilled artisan. Given the teachings of the prior art and the level of skill of the ordinary skilled artisan at the time of applicants' invention, it must be considered, Absent evidence to the contrary, that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Claims 63-64 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kovesdi et al. in view of Mulvihill et al. (US 5,648,254).

Applicants claim a DNA plasmid comprising an inducible promoter operably linked to nucleotide sequences encoding cytotoxic gene products of adenoviral E4 and E2A gene regions. Applicants also claim a DNA plasmid comprising an adenoviral gene fragment E4 open reading frame operably linked to an inducible promoter and which further expresses an adenoviral E2A gene fragment operably linked to an inducible promoter.

Kovesdi et al. is applied as in the above 35 USC 102(e) rejection. Kovesdi et al. does not recite placing the adenoviral E4 and E2A gene sequences on a single DNA plasmid.

Mulvihill et al. (issued 7/15/1997, priority to 12/4/1989, see whole document, particularly Column 2, Claims 1, 3, etc.) teaches the desirability of introducing multiple genes or coding regions into mammalian cells using a single DNA vector.

The ordinary skilled artisan, seeking to generate the packaging cell lines capable of expressing E1, E4 and E2 as taught by Kovesdi et al., would have been motivated to

include the adenoviral genes such as E4 and E2A on a single vector or plasmid, as taught by Mulvihill et al., rather than on two separate vectors so as to eliminate the need for multiple transfections of cells with multiple vectors. It would have been obvious for the ordinary skilled artisan to do this because including multiple genes or coding regions on a single vector streamlines the procedure for generating packaging cell lines and eliminates the need for multiple transfection steps. Given the teachings of the prior art and the level of skill of the ordinary skilled artisan at the time of applicants' invention, it must be considered, absent evidence to the contrary, that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

35 USC 112, 1st Paragraph Rejections

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 42 and 51 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

This rejection is maintained for reasons of record and for reasons outlined below.

Applicants responded to this rejection by submitting a deposit declaration on 12/10/99. The deposit declaration is not sufficient to overcome the outstanding rejection

because the designation of the plasmid deposited under ATCC Accession Number 97325 in the deposit declaration differs from the plasmid recited as being deposited at the ATCC under Accession Number 97325 in claim 42. Specifically the plasmid recited in the declaration is designated as "pIK6.1 MIP (α)ORF6" but the plasmid recited in claim 42 is designated as "pIK6.1 MIP(α) –E4 ORF6". It is unclear if these represent the same plasmid. Also, on p. 8 of the instant specification, applicants recite the pIK6.1 MIP(α) – E2A plasmid as being deposited at the ATCC under the same Accession Number (97325) as the pIK6.1 MIP (α)ORF6 and pIK6.1 MIP(α) –E4 ORF6 plasmids. It is unclear what is deposited under ATCC Accession Number 97325.

The designation of ATCC 11990 is applied to the plasmid pIK6.1 MIP(α) – E2A on p. 15 of the instant specification ***and*** to the packaging cell line 293-E1/ORF6 on p. 23 of the instant specification, while it is listed as pertaining to the 293 cell line carrying the Ad5 E4 ORF6 DNA gene fragment in the deposit declaration on 12/10/99.

35 USC 112, 2nd Paragraph Rejections

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 41 and 49-51 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 41 is vague in that while it depends from a claim (38) which limits the promoter to those associated with cAMP response element binding protein regulated

genes, claim 41 recites a tetracycline responsive promoter which does not appear to be a promoter associated with cAMP response element binding protein regulated genes.

Claims 49-51 are vague in the recitation of the phrase "derived from a 293 cell" or "derived from human embryonic kidney cells" because it is unclear how closely related the claimed derived cells are to the starting cells. Because the steps involved in the derivation of the claimed cells from the starting cell lines are not recited, the metes and bounds of the claimed packaging cells are unclear.

Claim Objections

Claim 41 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. The tetracycline responsive promoter recited in Claim 41 does not appear to be a promoter selected from cAMP response element binding protein regulated gene, as required by claim 38.

No Claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Guzo, Ph.D., whose telephone number is (571) 272-0767. The examiner can normally be reached on Monday-Thursday from 8:00 AM to 5:30 PM. The examiner can also be reached on alternate Fridays

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Chris Low, Ph.D., can be reached on (571) 272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

December 31, 2008

/David Guzo/
Primary Examiner
Art Unit 1636